In the claims:

Please amend the claims as shown below:

- 1. (Currently Amended) A method of identifying a drug that inhibits growth or replication of a cell having a mutated MAD2 gene or an analog or homolog thereof, said method comprising the steps of:
 - (a) identifying a secondary gene comprising:
 - (1) providing a plurality of cells having a genome, which includes at least one mutated MAD2 gene or homolog thereof;
 - (2) effecting one or more mutations in the genome of said cells, at one or more secondary genes;
 - (3) selecting those cells having at least one mutation that proves lethal to said cells only when said mutated MAD2 gene is present;
 - (4) determining a site in the genome of said cells in which said at least one lethal mutation is located, to provide a secondary gene;
 - (a-b) contacting a cell having a mutated MAD2 gene or an analog or homolog thereof with a drug; and
 - (b-c) identifying said drug by determining whether the drug modulates the activity of a the wildtype secondary gene identified in step (a), such that the drug is lethal to said cell having a mutated MAD2 gene but not to a wild type cell which is synthetically lethal when it is mutated and is present in combination with mutated MAD2 gene or analog or homolog thereof.
- 2. (Previously Presented) The method of claim 1 in which the cell is a tumor cell.

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- 3. (Previously Presented) The method of claim 1, comprising the further step of comparing the results of step (b) with a control cell grown without the drug.
- 4. (Previously Presented) The method of claim 3 in which the control cell is a normal cell.
- 5. (Previously Presented) The method of claim 3 in which the control cell is a tumor cell.
- 6. (Previously Presented) The method of claim 3 in which the control cell has a mutated MAD2 gene or an analog or homolog thereof.
- 7. (Currently Amended) The method of claim 1 in which the secondary gene is <u>TUB1 or</u> selected from the group consisting of analogs and homologs TUB1, CIN8, SFI1, STU1 and combinations thereof.
- 8. (Withdrawn) A method of identifying a compound useful in the treatment of tumor cells having a mutated MAD2 gene or homolog or analog thereof which comprises the steps of:
 - (a) contacting a secondary gene product, which in its mutant form is synthetically lethal in combination with a mutated MAD2 gene or homolog or analog thereof, with a test compound and
 - (b) determining the activity of the secondary gene product.
- 9. (Withdrawn) The method of claim 8, comprising the further step of comparing the activity of the secondary gene product in the presence of the test compound with the activity of the gene product in the absence of the secondary gene product.
- 10. (Withdrawn) The method of claim 8 in which the secondary gene is selected from the group consisting of analogs and homologs TUB1, CIN8, SFI1, STU1 and combinations thereof.

- 11. (Withdrawn) A screening assay system for identifying a drug, comprising:
 - (a) the control yeast cell having a deletion in MAD2 gene, analog or homolog thereof and a wildtype secondary gene in which its mutant form is synthetically lethal in combination with a deletion of MAD2;
 - (b) a test yeast cell system comprising the drug and the yeast with the MAD2 delection; and
 - (c) a detector for comparing the viability of MAD2 in the test system compared to the control system where a decrease in viability of the test cell system identifies positive drug candidates.
- 12. (Withdrawn) A method of screening for the presence of benign or malignant cell growth in a tissue sample comprising the steps of:
 - (a) providing a tissue sample from an individual suspected of having cancer;
 - (b) assessing the expression of MAD2 in the cells of the tissue sample; and
 - (c) comparing the MAD2 expression of the tissue sample with the MAD2 expression of a control sample, wherein the presence of aberrant expression of MAD2 in the test sample as compared with expression in the control sample is indicative of the presence of carcinoma.
- 13. (Withdrawn) A pharmaceutical composition comprising an effective amount of a drug and a pharmaceutically acceptable carrier or diluent, said drug capable of selectively interacting with at least one secondary gene or gene product in a target cell which comprises a mutated or deleted primary MAD2 gene or gene product, whereby the exposure of the target cell to the drug arrests cell division or selectively kills cells.
- 14. (Withdrawn) The pharmaceutical composition of claim 13 wherein said drug comprises oligonucleotide, gene product, homologs or analogs of oligonucleotide or gene product, a small molecule, or a peptide mimetic.

- 15. (Withdrawn) A method for treating a human or animal hosting or susceptible of hosting a disease associated with MAD2 mutation which comprises providing the pharmaceutical composition of claim 13 and treating said human or animal with an effective amount of the pharmaceutical composition.
- (Withdrawn) The method of claim 13 in which the disease is selected from the group 16. consisting of apudoma, choristoma, branchioma, malignant carcinoid syndrome, carcinoid heart disease, carcinoma (e.g., Walker, basal cell, basosquamous, Brown-Pearce, ductal, Ehrlich tumor, Krebs 2, merkel cell, mucinous, non-small cell lung, oat cell, papillary, scirrhous, bronchiolar, bronchogenic, squamous cell, and transitional cell), histiocytic disorders, leukemia (e.g., B-cell, mixed-cell, null-cell, T-cell, T-cell chronic, HTLV-II-associated, lymphocytic acute, lymphocytic chronic, mast-cell, and myeloid), histiocytosis malignant, Hodgkin's disease, immunoproliferative small, non-Hodgkin's lymphoma, plasmacytoma, reticuloendotheliosis, melanoma, chondroblastoma, chondroma, chondrosarcoma, fibroma, fibrosarcoma, giant cell tumors, histiocytoma, lipoma, liposarcoma, mesothelioma, myxoma, myxosarcoma, osteoma, osteosarcoma, Ewing's sarcoma, synovioma, adenofibroma, adenolymphoma, carcinosarcoma, chordoma, craniopharyngioma, dysgerminoma, hamartoma, mesenchymoma, mesonephroma, myosarcoma, ameloblastoma, cementoma, odontoma, teratoma, thymoma, trophoblastic tumor, adenocarcinoma, adenoma, cholangioma, cholesteatoma, cylindroma, cystadenocarcinoma, cystadenoma, granulosa cell tumor, gynandroblastoma, hepatoma, hidradenoma, islet cell tumor, Leydig cell tumor, papilloma, sertoli cell tumor, theca cell tumor, leiomyoma, leiomyosarcoma, myoblastoma, myoma, myosarcoma, rhabdomyoma, rhabdomyosarcoma, ependymoma, ganglioneuroma, glioma, medulloblastoma, meningioma, neurilemmoma, neuroblastoma, neuroepithelioma, neurofibroma, neuroma, paraganglioma, paraganglioma nonchromaffin, angiokeratoma, angiolymphoid hyperplasia with eosinophilia, angioma sclerosing, angiomatosis, glomangioma, hemangioendothelioma, hemangioma, hemangiopericytoma, hemangiosarcoma, lymphangioma, lymphangiosarcoma, pinealoma, carcinosarcoma, chondrosarcoma, cystosarcoma phyllodes, fibrosarcoma, hemangiosarcoma, leiomyosarcoma, leukosarcoma, liposarcoma, lymphangiosarcoma,

myosarcoma, myxosarcoma, ovarian carcinoma, rhabdomyosarcoma, sarcoma, neurofibromatosis, cervical dysplasia, fibrosis, benign prostate hyperplasia, atherosclerosis, restenosis, glomulerosclerosis, cheloid, psoriasis, lentigo, keratosis, achrochordon, molluscum contagiosum, venereal warts, sebaceous hyperplasia, condylomata acuminatum, angioma, venous lakes, chondrodermatitis, granuloma pyogenicum, hidradenitis suppurativa, keloids, keratoacanthoma, leukoplakia, steatocystoma multiplex, trichiasis, superficial epithelial nevus, polyp, junctional nevus, pyogenic granuloma, prurigo nodularis, dermatofibroma, adenoma sebaceum, papilloma, and combinations thereof.

- 17. (Withdrawn) The method, according to claim 15, wherein the disease comprises yeast infection.
- 18. (Withdrawn) The method of claim 15, wherein the disease comprises breast cancer.
- 19. (Withdrawn) A method of treating cancer cells having abnormal accumulation of MAD2 gene or an analog or homolog thereof which comprises administering a pharmaceutical composition comprising an effective amount of an agent and a pharmaceutically acceptable carrier or diluent, said agent capable of selectively interacting with at least one secondary gene or gene product that is found in a cell having at least one primary gene defect, wherein said gene product is selected from (or wherein said lethal gene codes for) a human isozyme TUB1, CIN8, SFI1, STU1 and combinations thereof.
- 20. (Withdrawn) A recombinant eukaryotic cell comprising at least one secondary gene and at least one primary gene MAD2, or analog or homolog thereof, wherein said primary gene MAD2 is mutated such that the up-regulation, down-regulation, elimination, or disruption of said secondary gene results in synthetic lethality.
- 21. (Withdrawn) The recombinant eukaryotic cell of claim 20 in which at least one secondary gene or product thereof is selected from the group consisting of analogs and homologs TUB1, CIN8, SFI1, STUI and combinations thereof.

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22. (Withdrawn) The recombinant eukaryotic cell of claim 20 in which the primary gene is eliminated or disrupted.